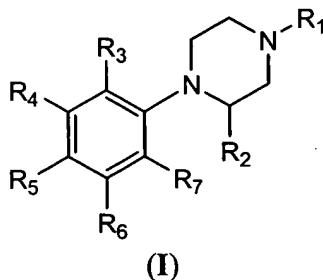


Version with markings to show changes made.

1. (original) A compound of Formula (I):



wherein:

R₁ is H or C₁₋₈ alkyl;

R₂ is C₂₋₄ alkenyl, C₁₋₄ alkyl or C₁₋₄ haloalkyl; and

R₃, R₄, R₅, R₆ and R₇ are each independently H, C₁₋₄ acyl, C₁₋₄ acyloxy, C₁₋₄ acylthioxy, C₂₋₄ alkenyl, C₁₋₄ alkoxy, C₁₋₄ alkyl, C₁₋₄ alkylcarboxamido, C₁₋₄ alkylsulfinyl, C₁₋₄ alkylsulfonamide, C₁₋₄ alkylsulfonyl, C₁₋₄ alkylthio, amino, C₁₋₄ alkylamino, carbo-C₁₋₄-alkoxy, carboxamide, cyano, C₂₋₆ dialkylamino, C₁₋₄ haloalkoxy, C₁₋₄ haloalkyl, C₁₋₄ haloalkylsulfinyl, C₁₋₄ haloalkylsulfonyl, C₁₋₄ haloalkylthio, halogen, hydroxyl, phenyl, and thiol; or

a pharmaceutically acceptable salt, hydrate and solvate thereof;

provided that the compound is not 1-(4-Chloro-phenyl)-2-methyl-piperazine; 1-(3,5-Difluoro-phenyl)-2-methyl-piperazine; 2-Methyl-1-(2-methylsulfanyl-phenyl)-piperazine; 4-Amino-3-fluoro-2-(2-methyl-piperazin-1-yl)-5-nitro-benzonitrile; 2-Methyl-1-phenyl-piperazine; 4-(2-Isopropyl-piperazin-1-yl)-2-trifluoromethyl-benzonitrile; 4-(2-Ethyl-piperazin-1-yl)-2-trifluoromethyl-benzonitrile; 4-(2-Methyl-piperazin-1-yl)-2-trifluoromethyl-benzonitrile; 1-(3-Chloro-phenyl)-2-methyl-piperazine; 2-Methyl-1-m-tolyl-piperazine; 4-(2-Methyl-piperazin-1-yl)-benzamide; 1-(2-Fluoro-phenyl)-2-methyl-piperazine; 4-(2-Methyl-piperazin-1-yl)-phenol; 1-(3-Methoxy-phenyl)-2-methyl-piperazine; 2-Methyl-1-(3-trifluoromethyl-phenyl)-piperazine; 1-(4-Methoxy-phenyl)-2-methyl-piperazine; 2-Methyl-1-p-tolyl-piperazine; 2,4-Dimethyl-1-phenyl-piperazine; 4-Chloro-5-(4-ethyl-2-methyl-piperazin-1-yl)-benzene-1,2-diamine; 4-Chloro-5-(4-ethyl-2-methyl-piperazin-1-yl)-2-nitro-

phenylamine; 5-(4-Ethyl-2-methyl-piperazin-1-yl)-2-nitro-4-trifluoromethyl-phenylamine; and 5-(4-Ethyl-2-methyl-piperazin-1-yl)-4-methyl-2-nitro-phenylamine.

2. (original) The compound according to claim 1 wherein R₁ is H.

3. (original) The compound according to claim 1 wherein R₁ is C₁₋₈ alkyl.

Claims 4 to 8 have been canceled.

9. (amended) The compound according to ~~any one of claims~~ claim 1 to 8 wherein R₂ is C₂₋₄ alkenyl.

Claim 10 has been canceled.

11. (amended) The compound according to ~~any one of claims~~ claim 1 to 8 wherein R₂ is C₁₋₄ alkyl.

12. (amended) The compound according to ~~any one of claims~~ claim 1 to 8 wherein R₂ is methyl.

Claims 13 to 16 have been canceled.

17. (amended) The compound according to ~~any one of claims~~ claim 1 to 16 wherein R₃, R₄, R₅, R₆ and R₇ are each independently selected from the group consisting of H, C₁₋₄ alkoxy, C₁₋₄ alkyl, cyano, C₁₋₄ haloalkoxy, C₁₋₄ haloalkyl and halogen.

Claim 18 has been canceled.

19. (original) The compound according to claim 17 wherein R₃, R₄, R₅, R₆ and R₇ are each independently selected from the group consisting of H, C₁₋₄ haloalkoxy, C₁₋₄ haloalkyl and halogen.

20. (original) The compound according to claim 17 wherein R_3 , R_4 , R_5 , R_6 and R_7 are each independently selected from the group consisting of H, CH_3 , CH_2CH_3 , $CH(CH_3)_2$, cyano, OCF_3 , CF_3 , F, Cl and Br.
21. (original) The compound according to claim 17 wherein R_3 , R_4 , R_5 , R_6 and R_7 are each independently selected from the group consisting of H, CF_3 , F, Cl and Br.
22. (amended) The compound according to ~~any one of claims~~ claim 1 to 16 wherein R_3 is H or F.
23. (amended) The compound according to ~~any one of claims~~ claim 1 to 16 and 22 wherein R_4 is selected from the group consisting of H, cyano, F, Cl and Br.
24. (amended) The compound according to ~~any one of claims~~ claim 1 to 16, 22 and 23 wherein R_5 is selected from the group consisting of H, CH_3 , $CH(CH_3)_2$, OCF_3 , CF_3 , F, Cl and Br.
25. (amended) The compound according to ~~any one of claims~~ claim 1 to 16 and 22 to 24 wherein R_6 is selected from the group consisting of H, F, Cl and Br.
26. (amended) The compound according to ~~any one of claims~~ claim 1 to 16 and 22 to 25 wherein R_7 is selected from the group consisting of H, CH_3 , F, Cl and Br.
27. (original) The compound of claim 1 selected from the group consisting of:
1-(2,3-Difluoro-phenyl)-2-ethyl-piperazine;
1-(3-Fluoro-phenyl)-2-ethyl-piperazine;
1-(4-Fluoro-phenyl)-2-ethyl-piperazine;
(R)-1-(3-Chloro-4-fluoro-phenyl)-2-methyl-piperazine;
(S)-1-(3-Chloro-4-fluoro-phenyl)-2-methyl-piperazine;
(R)-1-(3,4-Difluoro-phenyl)-2-methyl-piperazine;
(S)-1-(3,4-Difluoro-phenyl)-2-methyl-piperazine;
(R)-1-(3-Chloro-2-fluoro-phenyl)-2-methyl-piperazine;
(S)-1-(3-Chloro-2-fluoro-phenyl)-2-methyl-piperazine;
(R)-1-(4-Fluoro-phenyl)-2-methyl-piperazine;

(S)-1-(4-Fluoro-phenyl)-2-methyl-piperazine;
(R)-1-(3,4-Dichloro-phenyl)-2-methyl-piperazine;
(S)-1-(3,4-Dichloro-phenyl)-2-methyl-piperazine;
(R)-1-(3-Chloro-4-methyl-phenyl)-2-methyl-piperazine;
(S)-1-(3-Chloro-4-methyl-phenyl)-2-methyl-piperazine;
(R)-1-(3,4-Difluoro-phenyl)-2-methyl-piperazine;
(S)-1-(3,4-Difluoro-phenyl)-2-methyl-piperazine;
(R)-1-(3,5-Dichloro-phenyl)-2-methyl-piperazine;
(S)-1-(3,5-Dichloro-phenyl)-2-methyl-piperazine;
(R)-1-(2,5-Difluoro-phenyl)-2-methyl-piperazine;
(S)-1-(2,5-Difluoro-phenyl)-2-methyl-piperazine;
(R)-1-(4-Chloro-3-fluoro-phenyl)-2-methyl-piperazine;
(S)-1-(4-Chloro-3-fluoro-phenyl)-2-methyl-piperazine;
(R)-1-(3-Chloro-2-methyl-phenyl)-2-methyl-piperazine;
(S)-1-(3-Chloro-2-methyl-phenyl)-2-methyl-piperazine;
(R)-1-(5-Chloro-2-fluoro-phenyl)-2-methyl-piperazine;
(S)-1-(5-Chloro-2-fluoro-phenyl)-2-methyl-piperazine;
(R)-1-(5-Chloro-2-methyl-phenyl)-2-methyl-piperazine;
(S)-1-(5-Chloro-2-methyl-phenyl)-2-methyl-piperazine;
1-(3-Chloro-4-fluoro-phenyl)-2-ethyl-piperazine;
1-(3-Chloro-phenyl)-2-ethyl-piperazine;
1-(4-Chloro-phenyl)-2-ethyl-piperazine;
1-(3,4-Difluoro-phenyl)-2-ethyl-piperazine and
(R)-1-(5-Chloro-2-fluoro-phenyl)-2-ethyl-piperazine;
or a pharmaceutically acceptable salt, hydrate and solvate thereof.

28. (original) The compound of claim 1 selected from the group consisting of:

(R)-1-(2-Fluoro-5-trifluoromethyl-phenyl)-2-methyl-piperazine;
(S)-1-(2-Fluoro-5-trifluoromethyl-phenyl)-2-methyl-piperazine;
(R)-1-(4-Chloro-2-fluoro-phenyl)-2-methyl-piperazine;
(S)-1-(4-Chloro-2-fluoro-phenyl)-2-methyl-piperazine;
(R)-1-(3-Chloro-5-fluoro-phenyl)-2-methyl-piperazine;
(S)-1-(3-Chloro-5-fluoro-phenyl)-2-methyl-piperazine;

(R)-1-(3-Fluoro-phenyl)-2-methyl-piperazine;
(S)-1-(3-Fluoro-phenyl)-2-methyl-piperazine;
(R)-1-(2-Fluoro-4-trifluoromethyl-phenyl)-2-methyl-piperazine;
(S)-1-(2-Fluoro-4-trifluoromethyl-phenyl)-2-methyl-piperazine;
(R)-1-(2-Chloro-3-fluoro-phenyl)-2-methyl-piperazine;
(S)-1-(2-Chloro-3-fluoro-phenyl)-2-methyl-piperazine;
(R)-1-(2-Fluoro-5-methyl-phenyl)-2-methyl-piperazine;
(S)-1-(2-Fluoro-5-methyl-phenyl)-2-methyl-piperazine;
(R)-1-(4-Fluoro-biphenyl-3-yl)-2-methyl-piperazine;
(S)-1-(4-Fluoro-biphenyl-3-yl)-2-methyl-piperazine;
(R)-1-(2,5-Difluoro-4-methoxy-phenyl)-2-methyl-piperazine;
(S)-1-(2,5-Difluoro-4-methoxy-phenyl)-2-methyl-piperazine;
(R)-1-(2-Fluoro-4-methyl-phenyl)-2-methyl-piperazine;
(S)-1-(2-Fluoro-4-methyl-phenyl)-2-methyl-piperazine;
(R)-1-(2-Chloro-5-fluoro-phenyl)-2-methyl-piperazine;
(S)-1-(2-Chloro-5-fluoro-phenyl)-2-methyl-piperazine;
(R)-1-(2-Chloro-4-fluoro-phenyl)-2-methyl-piperazine;
(S)-1-(2-Chloro-4-fluoro-phenyl)-2-methyl-piperazine;
(R)-1-(2,4-Dichloro-phenyl)-2-methyl-piperazine;
(S)-1-(2,4-Dichloro-phenyl)-2-methyl-piperazine;
(R)-1-(2,5-Dichloro-phenyl)-2-methyl-piperazine;
(S)-1-(2,5-Dichloro-phenyl)-2-methyl-piperazine;
(R)-1-(3,5-Bis-trifluoromethyl-phenyl)-2-methyl-piperazine;
(S)-1-(3,5-Bis-trifluoromethyl-phenyl)-2-methyl-piperazine;
(R)-1-(4-Fluoro-2-methyl-phenyl)-2-methyl-piperazine;
(S)-1-(4-Fluoro-2-methyl-phenyl)-2-methyl-piperazine;
(R)-1-(2-Chloro-phenyl)-2-methyl-piperazine;
(S)-1-(2-Chloro-phenyl)-2-methyl-piperazine;
(R)-1-(2,3-Dichloro-phenyl)-2-methyl-piperazine;
(R)-1-(2,3-Dichloro-phenyl)-2-methyl-piperazine;
(R)-1-(2,6-Dichloro-phenyl)-2-methyl-piperazine;
(R)-1-(2,6-Dichloro-phenyl)-2-methyl-piperazine;
(R)-1-(2-Chloro-5-trifluoromethyl-phenyl)-2-methyl-piperazine;

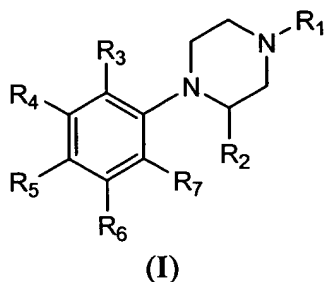
(R)-1-(2-Chloro-5-trifluoromethyl-phenyl)-2-methyl-piperazine;
(R)-2-Methyl-1-(4-trifluoromethyl-phenyl)-piperazine;
(S)-2-Methyl-1-(4-trifluoromethyl-phenyl)-piperazine;
(R)-1-(2-Fluoro-3-trifluoromethyl-phenyl)-2-methyl-piperazine;
(S)-1-(2-Fluoro-3-trifluoromethyl-phenyl)-2-methyl-piperazine;
(R)-1-(3-Fluoro-5-trifluoromethyl-phenyl)-2-methyl-piperazine;
(R)-1-(3-Fluoro-5-trifluoromethyl-phenyl)-2-methyl-piperazine;
(R)-1-(4-Chloro-3-trifluoromethyl-phenyl)-2-methyl-piperazine;
(S)-1-(4-Chloro-3-trifluoromethyl-phenyl)-2-methyl-piperazine; and
(R)-2,4-Dimethyl-1-(3-trifluoromethyl-phenyl)-piperazine;
or a pharmaceutically acceptable salt, hydrate and solvate thereof.

29. (original) The compound of claim 1 selected from the group consisting of:

1-(2-Bromo-phenyl)-2-vinyl-piperazine;
1-(4-Chloro-phenyl)-2-vinyl-piperazine;
1-(3-Fluoro-phenyl)-2-vinyl-piperazine;
1-(3-Chloro-4-fluoro-phenyl)-2-vinyl-piperazine;
1-(3-Chloro-phenyl)-2-vinyl-piperazine;
1-(3-Bromo-phenyl)-2-vinyl-piperazine;
1-(3,5-Dichloro-phenyl)-2-vinyl-piperazine;
1-(2-Bromo-4-isopropyl-phenyl)-2-vinyl-piperazine;
1-(2-Bromo-4-trifluoromethoxy-phenyl)-2-vinyl-piperazine;
1-(2-Bromo-4-trifluoromethyl-phenyl)-2-vinyl-piperazine;
3-(2-Vinyl-piperazin-1-yl)-benzonitrile;
1-(3,5-Difluoro-phenyl)-2-vinyl-piperazine;
1-*o*-Tolyl-2-vinyl-piperazine and
1-(2,3-Difluoro-phenyl)-2-vinyl-piperazine;
or a pharmaceutically acceptable salt, hydrate and solvate thereof.

30. (amended) The compound according to ~~any one of claims claim~~ claim 1 to 26 wherein said compound is an *R* enantiomer.

31. (amended) The compound according to ~~any one of claims~~ claim 1 to 26 wherein said compound is an *S* enantiomer.
32. (original) A pharmaceutical composition comprising a pharmaceutical acceptable carrier in combination with at least one compound according to Formula (I):



wherein:

- R₁ is H or C₁₋₈ alkyl;
R₂ is C₂₋₄ alkenyl, C₁₋₄ alkyl or C₁₋₄ haloalkyl; and
R₃, R₄, R₅, R₆ and R₇ are each independently H, C₁₋₄ acyl, C₁₋₄ acyloxy, C₁₋₄ acylthioxy, C₂₋₄ alkenyl, C₁₋₄ alkoxy, C₁₋₄ alkyl, C₁₋₄ alkylcarboxamido, C₁₋₄ alkylsulfinyl, C₁₋₄ alkylsulfonamide, C₁₋₄ alkylsulfonyl, C₁₋₄ alkylthio, amino, C₁₋₄ alkylamino, carbo-C₁₋₄-alkoxy, carboxamide, cyano, C₂₋₆ dialkylamino, C₁₋₄ haloalkoxy, C₁₋₄ haloalkyl, C₁₋₄ haloalkylsulfinyl, C₁₋₄ haloalkylsulfonyl, C₁₋₄ haloalkylthio, halogen, hydroxyl, phenyl, and thiol; or
a pharmaceutically acceptable salt, hydrate and solvate thereof.

33. (amended) A method of modulating a 5HT_{2C} receptor comprising contacting said receptor with a therapeutically effective amount of a compound as in ~~any one of claims~~ claim 1 to 31.
34. (original) The method according to claim 33 wherein said compound is an agonist of said receptor.
35. (amended) A method of prophylaxis or treatment of disorders of the central nervous system; damage to the central nervous system; cardiovascular disorders; gastrointestinal disorders; diabetes insipidus or sleep apnea comprising administering to an individual in need of such prophylaxis or treatment a therapeutically effective amount of a compound according to ~~any one of claims~~ claim 1 to 31 or a pharmaceutical composition according to claim 32.

36. (original) The method according to claim 35 wherein the disorders of the central nervous system are selected the group consisting of depression, atypical depression, bipolar disorders, anxiety disorders, obsessive-compulsive disorders, social phobias or panic states, sleep disorders, sexual dysfunction, psychoses, schizophrenia, migraine and other conditions associated with cephalic pain or other pain, raised intracranial pressure, epilepsy, personality disorders, Alzheimer disease, age-related behavioral disorders, behavioral disorders associated with dementia, organic mental disorders, mental disorders in childhood, aggressivity, age-related memory disorders, chronic fatigue syndrome, drug and alcohol addiction, obesity, bulimia, anorexia nervosa and premenstrual tension.

37. (original) The method according to claim 36 wherein the disorder of the central nervous system is obesity.

Claim 38 has been canceled.

39. (original) The method according to claim 36 wherein the sexual dysfunction is Male erectile dysfunction.

Claims 40 to 44 have been canceled.

45. (amended) The method according to claim ~~44~~ 37 or 39 wherein said ~~mammal individual~~ is a human.

46. (amended) A method of decreasing food intake of an individual comprising administering to said individual a therapeutically effective amount of a compound according to ~~any one of claims claim 1 to 31~~ or a pharmaceutical composition according to claim 32.

Claim 47 has been canceled.

48. (amended) The method according to claim ~~47~~ 46 wherein said ~~mammal individual~~ is a human.

49. (amended) A method of inducing satiety in an individual comprising administering to said individual a therapeutically effective amount of a compound according to ~~any one of claims~~ claim 1 to 31 or a pharmaceutical composition according to claim 32.

Claim 50 has been canceled.

51. (amended) The method according to claim ~~50~~ 49 wherein said ~~mammal~~ individual is a human.

52. (amended) A method of controlling weight gain of an individual comprising administering to said individual suffering from weight control a therapeutically effective amount of a compound according to ~~any one of claims~~ claim 1 to 31 or a pharmaceutical composition according to claim 32.

Claim 53 has been canceled.

54. (amended) The method according to claim ~~53~~ 52 wherein said ~~mammal~~ individual is a human.

Claims 55 to 58 have been canceled.

59. (amended) A method of producing a pharmaceutical composition comprising admixing at least one compound according to ~~any one of claims~~ claim 1 to 31 and a pharmaceutically acceptable carrier.

Claims 60 to 78 have been canceled.

79. (new) The compound according to claim 1 wherein:
R₁ is H, methyl, ethyl, *n*-propyl, *iso*-propyl or *n*-butyl;
R₂ is a vinyl, methyl, ethyl, *n*-propyl, C₁₋₄ haloalkyl or -CF₃;
R₃ is H or F;
R₄ is selected from the group consisting of H, cyano, F, Cl and Br;
R₅ is selected from the group consisting of H, CH₃, CH(CH₃)₂, OCF₃, CF₃, F, Cl and Br;
R₆ is selected from the group consisting of H, F, Cl and Br; and

R₇ is selected from the group consisting of H, CH₃, F, Cl and Br.

80. (new) A method of treating a 5HT_{2C} receptor associated disorder comprising administering to an individual in need of such treatment an effective amount of a compound according to claim 1, or a pharmaceutical composition according to claim 32.

Remarks

The specification has been amended to add the "Cross Reference to related application" section showing that this application is claiming priority to an earlier US provisional application.

After entry of the above amendment, Claims 1-3, 9, 11, 12, 17, 19-37, 39, 45, 46, 48, 49, 51, 52, 54, 59, 79 and 80 will be pending in this application.

Pending Claims 1-3, 19-21, 27-29, 32, 34, 36, 37 and 39 are original claims.

Pending Claims 9, 11, 12, 17, 22-26, 30, 31, 33, 35, 45, 46, 48, 49, 51, 52, 54 and 59 have been amended. Many of these pending claims were amended to merely remove dependencies of multiple dependent claims that dependent from another multiple dependent claim.

Claim 45 was amended to depend from 37 or 39 and "mammal" was amended to "individual"; support for this amendment can be found in original claim 44 and throughout the specification.

Claim 48 was amended to depend from 46 and "mammal" was amended to "individual"; support for this amendment can be found in original claim 47 and throughout the specification.

Claim 51 was amended to depend from 49 and "mammal" was amended to "individual"; support for this amendment can be found in original claim 50 and throughout the specification.

Claim 54 was amended to depend from 52 and "mammal" was amended to "individual"; support for this amendment can be found in original claim 53 and throughout the specification.

Claims 4-8, 10, 13-16, 18, 38, 40-44, 47, 50, 53, 55-58 and 60-78 have been canceled without prejudice.

New Claims 79 and 80 have been added without introducing new matter. Support for new claims can be found throughout the application and claims as originally filed. Support for new Claim 79 can be found from original claims of which many have been canceled. Additional support can be found in the specification, for example, for R_1 see published PCT application page 17, lines 9 to 25; for R_2 see page 18, lines 2 to 15; for R_3 see page 19 lines 11 to 12; for R_4 see page 19, lines 15 to 16; for R_5 see page 19, lines 17 to 18, for R_6 see page 19, lines 21 to 22; and for R_7 see page lines 23 to 24. Support for new Claim 80 can be found throughout the specification, for example, page 1, lines 6 to 8, and also please see section entitled "Methods and Use" starting on page 43, line 2.


Appln. No.: PCT/US2004/019540
Preliminary Amendment Dated: December 16, 2005
Page 24 of 24

Docket No.: 68.US2.PCT

Applicants respectfully submitted that no new matter has been added by way of this amendment. The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16, 1.17, and 1.492 as required by this paper to Deposit Account No. 50-1441.

Respectfully submitted,

Date: December 16, 2005



Lyle W. Spruce, Ph.D.
Registration No. 53,631

Arena Pharmaceuticals, Inc.
6166 Nancy Ridge Drive
San Diego, CA 92121
Telephone: (858) 453-7200 x1425
Facsimile: (858) 677-0065